AF/1615

TRANSMITTAL OF APPEAL BRIEF (Large Entity)

Docket No. 2001-0878.ORI

Re Application Of: **Alexander James Wigmore**

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
09/831,681	May 10, 2001	Susan T. Tran	022476	1615	

Invention: **TREATMENT OF ALLERGIC CONDITIONS**

COMMISSIONER FOR PATENTS:

Transmitted herewith in triplicate is the Appeal Brief in this application, with respect to the Notice of Appeal filed on **December 22, 2004**

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Dated: **February 25, 2005**

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PATENT APPLICATION

ATTORNEY DOCKET NO. 2001-0878.ORI

UNITED STATES PATENT AND TRADEMARK OFFICE

Date	:	February 25, 2005
Re App	:	Alexander James Wigmore
Serial No.	:	09/831,681
Filed	:	May 10, 2001
Title	:	TREATMENT FOR ALLERGIC CONDITIONS
Art Unit	:	1615
Examining Attorney	:	Susan T. Tran

APPEAL BRIEF

Attn: Board of Appeals and Interferences

Appellant's Brief (37 C.F.R. §1.192)

This Appeal Brief is submitted in furtherance of the Notice of Appeal filed on December 22, 2004 and received by the USPTO on December 28, 2004 in the above-identified application.

This Brief contains the following items under the headings and in the order set forth below (37 C.F.R. §1.192(c)):

1. Real Party in Interest
2. Related Appeals and Interferences
3. Status of Claims
4. Status of Amendments
5. Summary of Invention
6. Issues
7. Grouping of Claims
8. Arguments
9. Appendix of Claims

1. **Real Party in Interest (37 C.F.R. § 1.192(c)(1))**:

The real party in interest with respect to the above patent application is Hewlett Healthcare Limited of Melbourne, Derby, United Kingdom.

2. **Related Appeals and Interferences (37 C.F.R. §1.192(c)(2))**:

There are no other appeals or interferences known that are related to the above patent application.

3. **Status of Claims (37 C.F.R. §1.192(c)(3))**:

The claims in the application are 1-36. Of these claims:

Claims 10-15 and 17-29 are withdrawn from further consideration;

Claims 6, 31, and 32 are cancelled

Claims 1-5, 7-9, 16, 30, and 33-36 are pending;

Claims 1-5, 7-9, 16, 30, and 33-36 stand rejected.

The claims on appeal are 1-5, 7-9, 16, 30, and 33-36.

4. **Status of Amendments (37 C.F.R. §1.192(c)(4))**:

Claims 1-5, 7-9, 16, 30, and 33-36 were finally rejected in an Office Action dated August 23, 2004.

5. **Summary of the Invention (37 C.F.R. §1.192(c)(5))**:

The present invention concerns an oral drug composition for treating food allergies in human patients by delivering the drug at the small intestine and

preferably at the upper jejunum portion of the small intestine. The composition includes a chromone drug and a disintegrant, with the disintegrant material being present at a critical concentration in order to effect rapid dissolution of the composition and release of the chromone drug upon exposure to intestinal fluid.

Accordingly, the composition is prepared so that not more than 10% of the chromone dissolves after 2 hours of exposure to simulated gastric fluid, and so that at least 15% of the chromone dissolves within 10 minutes of subsequent exposure of the composition to simulated intestinal fluid (page 4, lines 7-15 of the PCT application publication no. WO 00/27392 ("the application")). To effect the rapid dissolution upon exposure to simulated intestinal fluid, the composition includes a ratio of disintegrant material to chromone by weight of at least 1.2:1 (page 13, lines 22-25). Various disintegrant materials may be utilized in the composition of the present invention, with such disintegrant materials being described in the application at page 15, line 22 - page 16, line 21.

6. Issues (37 C.F.R. §1.192(c)(6)):

A. Is the rejection of Claims 1-5, 7-9, 16, 30, and 33-36 under 35 U.S.C. §112, first paragraph, as failing to comply with written description requirement proper?

B. Is the rejection of Claims 1-5, 7-9, 16, 30, and 33-36 under 35 U.S.C. §103(a) as being unpatentable over Watts et al. (U.S. 6,200,602) proper?

7. Grouping of Claims (37 C.F.R. §1.192(c)(7)):

For the purposes of this appeal, the rejected claims do not stand or fall together. For each ground of rejection, the appealed claims fall into the following groups:

I. Claims 1-5, 7, 9, 16, 30, and 33;

II. Claim 8;

III. Claim 34; and

IV. Claims 35 and 36.

8. Argument (37 C.F.R. §1.192(c)(8)):

A. Applicant's Claims 1-5, 7-9, 16, 30, and 33-36 fulfill the written description requirement of 35 U.S.C. § 112, first paragraph.

Applicant respectfully submits that all appealed claims are supported by the specification as originally filed, and further clarified in the Declaration under 37 C.F.R. §1.132 submitted on May 29, 2003. However, each group of claims identified in Section 7 hereinabove find distinct sets of supporting documentation under 35 U.S.C. §112, and are therefore separately patentable. Therefore, should any one of Groups I-IV be considered by the Board to not be properly supported under §112, its rejection should

not obscure a de novo review of the remaining claim groups. The Examiner has finally rejected Claims 1-5, 7-9, 16, 30, and 33-36 under 35 U.S.C. §112, first paragraph, and has asserted that the specification does not provide support for the pending claims, and particularly for the recited chromone dissolution rates in simulated intestinal fluid.

1. The specification as originally filed provides support for the claimed dissolution rates at page 4, lines 7-15.

Claim 1 of Group I recites a composition including a chromone wherein at least 15% of the chromone dissolves within 10 minutes of exposure of the composition to simulated intestinal fluid. The application at page 4, lines 11-15 explicitly describe the claimed chromone dissolution rate in simulated intestinal fluid in stating "from 15% ... of the chromone dissolves within 10 ... minutes of subsequent exposure of the composition to simulated intestinal fluid". Claim 34 of Group III is also explicitly described in such passage of the application as originally filed by stating that "from ... 80% ... of the chromone dissolves within ... 5 ... minutes of subsequent exposures of the composition to simulated intestinal fluid". The dissolution recitation in Claim 34 merely represents one embodiment of the many embodiments described

at page 4, lines 7-15 of the application, with the dissolution rates being related to the concentration ratio of disintegrant to chromone in the claimed composition. For example, the concentration ratio of disintegrant to chromone in Claim 34 is at least 1.4:1, specifically of microcrystalline cellulose to chromone. At such a concentration ratio, the chromone dissolution rate in simulated intestinal fluid is at least about 80% within about 5 minutes of exposure of the composition to simulated intestinal fluid. The embodiment recited in Claim 1 includes a disintegrant to chromone ratio of at least 1.2:1, which corresponds to a chromone dissolution rate of at least 15% within 10 minutes of exposure of the composition to simulated intestinal fluid.

The Examiner states in the Official Action dated August 23, 2004 that the specification does not provide support for the limitation "at least about 80% of the chromone dissolves within about 5 minutes", since the specification discloses a lower limit as low as 15%. It is well established law that an applicant need not claim all that he is entitled to claim, and that there is no requirement that the Applicant demonstrate the criticality of a lower limit in a particular claim to meet the description requirement (see In re Eichmeyer, 602 F.2d 974,

981 (CCPA 1979)). Moreover, it has been held that the written description of a broad range of characteristics adequately supports claims to a narrower range thereof (In re Wertheim, 541 F.2d 257, 265 (CCPA 1976)). The presently pending claims, and specifically Claim Groups III and IV, represent relatively narrow claims in view of the broad range described at page 4 of the specification. Namely, the chromone dissolution rate of about 80% within about 5 minutes in Claim 34 is within the described range of between 15 and 100% dissolution within between 1 and 30 minutes, as described at page 4, lines 11-15 of the specification.

The Court in In re Wertheim, 541 F.2d 257, 265 (CCPA 1976) dealt with a parent application describing a material concentration of 25 to 60% with specific examples of 36% and 50%. The claims in question in In re Wertheim specify a concentration of "between 35% and 60%". The Court held that the Patent and Trademark Office failed to establish a prima facie case of noncompliance with the written description requirement under §112 (In re Wertheim, 541 F.2d at 265). Contrary, therefore, to the Examiner's assertion in the Official Action of August 23, 2004, the In re Wertheim ruling demonstrates that a claim range may be

duly supported under 35 U.S.C. §112 even though it may not encompass the lower limit described in the specification.

This doctrine is further set forth in Kolmes v. World Fibers Corp., 107 F.3d 1534 (Fed. Cir. 1997), wherein the Court found that a claim limitation of "8-12 turns per inch" is well supported by the specification which discloses a rate of "4-12 turns per inch" Id. at 1539. It clearly follows that the presently pending claims, which recite dissolution rates within the ranges described in the specification as originally filed, are adequately supported thereby under 35 U.S.C. §112, first paragraph. As such, the claim recitation of "at least about 27%" and "at least about 21%" of chromone dissolution in Claims 35 and 36, respectfully, find adequate support in the specification as originally filed at page 4, lines 7-15.

In addition to the above, the Declaration of Alexander James Wigmore, filed on May 29, 2003, provides supplemental data for the dissolution of chromone upon exposure of the composition to simulated intestinal fluid. Specifically, page 5 of the Wigmore Declaration defines five distinct blends having different disintegrant to chromone ratios, wherein Batch 2 represents a 1.2:1 disintegrant to chromone ratio, and Batch 3 represents a 1.4:1 disintegrant to chromone ratio. As shown on pages 7 and 8 of the Wigmore

Declaration, through either a paddle or basket method, the claim limitations contained in the pending claims are reinforced by experimental results. For example, at a disintegrant to chromone ratio of 1.2:1 (Batch 2), 87.1% of the chromone dissolved within 10 minutes of exposure in a paddle method, and 93.4% of the chromone dissolved within 10 minutes in the basket method, wherein the disintegrant utilized was microcrystalline cellulose. Such results demonstrate that, in a composition having a disintegrant to chromone concentration ratio of 1.2:1, at least 15% of the chromone dissolves within 10 minutes of exposure of the composition to simulated intestinal fluid, as is recited in pending Claim 1. Moreover, "Batch 3", which represents a disintegrant to chromone ratio of 1.4:1, is demonstrated on pages 7 and 8 of the Wigmore Declaration as having 99.7 or 99.1% chromone dissolution within 5 minutes of exposure to simulated intestinal fluid, depending upon the method utilized. Such a chromone dissolution rate is clearly within the recited range of pending Claim 34.

In addition, the chromone dissolution rate recited in Claim Group IV are specifically demonstrated by the experimental results attached to Applicant's response dated April 30, 2004. Specifically, the composition recited in Claim 35 is demonstrated in the results by "Blend 2", such

that across each of formulations 1-4 in the attached experimental results, at least about 27% of the chromone dissolves within about 10 minutes of exposure of the composition to simulated intestinal fluid. Likewise, the composition recited in Claim 36 is analogous to that described with reference to "Blend 3" in the experimental results submitted on April 30, 2004. In each of the experiments conducted, Blend 3 had a chromone dissolution rate of at least about 21% within 5 minutes of exposure of the composition to simulated intestinal fluid. Accordingly, each of the claimed dissolution rates find specific and sufficient support in the specification as originally filed, and are clearly demonstrated in the experimental results provided on May 29, 2003 and April 30, 2004.

2. The specification as originally filed provides support under 35 U.S.C. §112, first paragraph for the claimed concentration ratios of disintegrant to chromone at page 13, line 22-25.

The specification as originally filed describes at page 13, lines 22-25 the preferred disintegrant to chromone ratios that provide the rapid dissolution of chromone in simulated intestinal fluid. This passage again defines a range of concentration ratios within which the pending claims define respective narrower ranges. Such a claim

methodology fully complies with 35 U.S.C. §112, first paragraph, and as described above with reference to In re Wertheim, 541 F.2d 257 (CCPA 1976) and Kolmes v. World Fibers Corp., 107 F.3d 1534 (Fed. Cir. 1997).

Moreover, the Wigmore Declaration submitted on May 29, 2003, and the experimental results attached to Applicant's response of April 30, 2004 specifically demonstrate obtaining the claimed chromone dissolution rate through the use of various disintegrant to chromone ratios, so long as such ratios are within the critical range of disintegrant to chromone ratios defined in the specification at page 13. As such, the claimed disintegrant to chromone concentration ratios are fully supported under 35 U.S.C. §112, first paragraph by the specification as originally filed.

3. The specification as originally filed provides support for the claimed disintegrant material at page 15, line 22 through page 16, line 21.

The Examiner asserts in the Official Action dated August 23, 2004 that the specification does not provide support for the disintegrants cited in Claims 1 and 34-36. However, Applicant submits that such disintegrant materials are specifically identified at page 15, line 22 through page 16, line 21.

In addition, the experimental results included in the Wigmore Declaration and attached to Applicant's response of April 30, 2004 demonstrate the utilization of the claimed disintegrant materials. In particular, the disintegrant materials recited in Claim Group IV are discussed with reference to the experimental results attached to Applicant's response of April 30, 2004. Namely, "Formulation 1" includes croscarmellose sodium, "Formulation 2" includes crosprovidone, "Formulation 3" includes sodium starch glycolate, and "Formulation 4" includes a combination of croscarmellose sodium and microcrystalline cellulose at a weight concentration ratio of 1:9 respectively. Such disintegrant materials are specifically recited in Claims 35 and 36 of Group IV.

As demonstrated above, the currently pending claims clearly find support in the specification as originally filed, and therefore comply with the requirements of 35 U.S.C. §112, first paragraph.

B. Appellant's Claims 1-5, 7-9, 16, 30, and 33-36 are unobvious and patentable over Watts et al. (U.S. 6,200,602).

The Watts et al. '602 patent is generally directed to a drug composition for delivery in the colon of the user. In particular, Watts et al. '602 disclose a composition

that prevents release of the drug until the formulation reaches the colon (column 6, lines 21-24).

1. The Watts et al. '602 fails to teach or suggest the claimed disintegrant to chromone ratios recited in each of Claim Groups I-IV.

The primary essence of the present invention is in providing an oral drug delivery composition that is formulated to pass through the patient's stomach substantially intact, and to subsequently rapidly disperse and dissolve upon exposure to intestinal fluid (see page 7, line 11 - page 8, line 2 of the application). As described in the above-cited passage, such rapid dissolution of the composition enables a relatively high concentration of the drug to be delivered to the upper portion of the small intestine where it can best treat allergic conditions relating to ingested substances.

A conventional enteric coating may optionally be utilized on the composition of the present invention to prevent premature dissolution while passing through the gastric fluid of the stomach. Once inside the intestinal fluid environment, the enteric coating dissolves, exposing the underlying composition of the present invention. At this point, the claimed disintegrant to chromone ratios enable the chromone to rapidly dissolve in the intestinal

fluid. Compositions of the prior art, by contrast, fail to rapidly disperse in the small intestine, possibly due to a gel that forms about the drug when exposed to intestinal fluid (page 3, lines 12-27 of the application; see also page 1 lines 21-23 of GB2,086,227 cited in Applicant's Information Disclosure Statement filed on July 9, 2001).

The gelling effect observed of drug delivery compositions of the prior art has been surprisingly overcome through the use of specific ratios of disintegrant material to the chromone that is present in the composition. In doing so, the chromone is allowed to rapidly disperse and dissolve in the intestinal fluid (see page 17, lines 10-23 of the application). Nowhere, however, do Watts et al. '602 teach or suggest the presently claimed ratios of disintegrant material to chromone.

(i) <u>The disintegrant material to chromone ratios recited in Claim Groups I-IV are critical to the operation of the invention</u>.

The Examiner argues that concentration differences between the present claims and the prior art do not support patentability unless there is evidence indicating that such concentration differences are critical. Here, the relative concentrations of the disintegrant to chromone in the

compositions of the present invention are indeed critical to the rapid dissolution characteristic that is central to the utility of the claimed compositions. Such criticality of the disintegrant to chromone ratios is described at page 17, lines 10-23 of the application, as well as in paragraph 5 of the Wigmore Declaration filed in Applicant's response of May 29, 2003. Specifically, Mr. Wigmore states that "the amount of disintegrant (for example microcrystalline cellulose) in the sodium cromoglycate tablet formulation was critical to the dissolution performance of the tablet." In reporting the findings represented in the present application, Mr. Wigmore stated on page 4 of his Declaration submitted on May 29, 2003 that it is critical to include a disintegrant to chromone ratio of at least 1.2 to 1 and more beneficially at least 1.4 or 1.5 to 1. "This is far in excess of the quantity of disintegrants conventionally used in tablets" (Wigmore Declaration submitted on May 29, 2003). The Applicant has clearly attested to the fact that the claimed disintegrant to chromone ratios are indeed critical to the compositions of the present invention.

2. The Watts et al. '602 fails to teach or suggest the chromone dissolution rates recited in Claim Groups I, III, and IV.

The Examiner argues on page 4 of the Official Action dated August 23, 2004 that the disclosure in Watts et al. '602 of an enteric coating material supports a prima facie case of obviousness, specifically in that the enteric coated tablet of Watts et al. '602 would have similar dissolution rates recited in the pending claims. Applicant submits, however, that the Examiner confuses the dissolution of the enteric coating with the presently claimed dissolution rates of the chromone. Specifically, an enteric coating incorporated over the compositions of the present invention would indeed likely have a similar dissolve rate in intestinal fluid as the enteric coating described in Watts et al. '602 (though Watts et al. '602 at column 6 lines 21-60 teaches the use of an enteric coating thickness that will not completely dissolve until the composition reaches the colon). The dissolution rate of an enteric coating, however, is independent of the dissolve rate of the drug itself, which drug, in the case of Watts et al. '602, is disposed underneath the enteric coating. Therefore, it is not the dissolve rate of an enteric coating that is now being claimed in the present application, but rather the dissolution rate of the

chromone drug itself into simulated intestinal fluid. Applicant respectfully submits that no teaching is found in Watts et al. '602 of the chromone dissolution rates now claimed. As stated above, the problem associated with compositions of the prior art that is now overcome by the present invention is the slow dissolution of the drug once it is exposed to intestinal fluid.

It is well established that the Examiner must establish a prima facie case of obviousness in order to support a claim rejection under 35 U.S.C. §103. "In rejecting claims under 35 U.S.C. §103 the Examiner bares the initial burden of presenting a prima facie case of obviousness" In re Rijckaert, 9 F.3d 1531, 1532 (Fed. Cir. 1993). The Court in In re Rijckaert further states that "[a] prima-facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art" In re Rijckaert, 9 F.3d at 1532. Here, since no suggestion is found in Watts et al. '602 of either the presently claimed critical disintegrant to chromone ratios or the chromone dissolution rates, the Examiner has failed to establish a prima facie case of obviousness. Only if the Examiner's initial burden of establishing a prima facie case of obviousness is met does

the burden of coming forward with evidence or argument shift to the applicant (In re Rijckaert, 9 F.3d at 1532). As such, Applicant bears no burden, as the Examiner argues, to demonstrate the properties of Watts et al. '602.

C. Conclusion

For the foregoing reasons, Claims 1-5, 7-9, 16, 30, and 33-36 are unobvious and patentable over the cited prior art. Applicant therefore submits that all pending claims are allowable on the merits and respectfully requests allowance thereof.

9. Appendix of Claims on Appeal (37 C.F.R. § 1.192(c)(9)):

1. An oral drug delivery composition comprising a chromone wherein (1) not more than 10% of the chromone dissolves after two hours exposure of the composition to simulated gastric fluid and (2) at least 15% of the chromone dissolves within 10 minutes of subsequent exposure of the composition to simulated intestinal fluid, said composition further comprising disintegrant at a ratio of at least 1.2:1 (w:w) of disintegrant to chromone wherein said disintegrant is selected from the group consisting of microcrystalline cellulose, croscarmellose sodium, crosprovidone, sodium starch glycolate, and combinations thereof.

2. A composition according to claim 1 wherein the composition is formulated as a tablet.

3. A composition according to claim 2 wherein the tablet has an enteric coating.

4. A composition according to claim 2 or 3 wherein the composition is still in the form of a tablet at the end of the exposure of the composition to gastric fluid.

5. The composition according to any one of claims 2 to 4 wherein the tablet comprises between about 50mg and 200mg of chromone.

7. A composition according to claim 1 wherein the composition comprises substantially spherical pellets of up to 5 mm diameter comprising the chromone, each pellet having an enteric coating.

8. An oral drug delivery composition comprising a chromone wherein the composition further comprises disintegrant at a ratio of at least 1.5:1 (w:w) of disintegrant to chromone.

9. A composition according to claim 1 or claim 8 wherein the ratio of disintegrant to chromone is between about 1.5:1 and 2.5:1

16. A composition according to any one of claims 1, 8, or 9 wherein the disintegrant is microcrystalline cellulose.

30. A composition according to any one of the preceding claims further comprising an amphoteric surfactant or a surfactant having a hydrophile-lipophile balance (HLB) value of less than about 10.

33. A composition according to any one of the preceding claims wherein the chromone is sodium cromoglycate.

34. An oral drug delivery composition comprising a chromone wherein (1) not more than 10% of the chromone dissolves after two hours exposure of the composition to simulated gastric fluid, and (2) at least about 80% of the chromone dissolves within about 5 minutes of subsequent exposure of the composition to simulated intestinal fluid, said composition further comprising microcrystalline cellulose at a ratio of at least 1.4:1 (w:w) of microcrystalline cellulose to chromone.

35. An oral drug delivery composition comprising a chromone wherein (1) not more than 10% of the chromone dissolves after two hours exposure of the composition to simulated gastric fluid, and (2) at least about 27% of the chromone dissolves within about 10 minutes of subsequent exposure of the composition to simulated intestinal fluid, said composition further comprising disintegrant at a ratio of at least 1.2:1 (w:w) of disintegrant to chromone,

wherein said disintegrant is selected from the group consisting of croscarmellose sodium, crosprovidone, sodium starch glycolate, and a blend of croscarmellose sodium and microcrystalline cellulose at a ratio of about 1:9 (w:w) of croscarmellose sodium to microcrystalline cellulose.

36. An oral drug delivery composition comprising a chromone wherein (1) not more than 10% of the chromone dissolves after two hours exposure of the composition to simulated gastric fluid, and (2) at least about 21% of the chromone dissolves within about 5 minutes of subsequent exposure of the composition to simulated intestinal fluid, said composition further comprising disintegrant at a ratio of at least 1.4:1 (w:w) of disintegrant to chromone, wherein said disintegrant is selected from the group consisting of super disintegrants in the form of a cross-linked cellulose, a cross-linked polymer, a cross-linked starch, and microcrystalline cellulose.

Respectfully submitted,

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Date: February 25, 2005

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CERTIFICATE OF MAILING

I hereby certify that the foregoing Appeal Brief in application Serial No. 09/531,681, filed May 10, 2001 of Alexander James Wigmore, entitled "TREATMENT OF ALLERGIC CONDITIONS" along with a transmittal cover letter are being deposited with the United States Postal Service as First Class mail, postage prepaid, in an envelope addressed to: Mail Stop Appeal Brief-Patents, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 25th day of February, 2005.

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Date of Signature: Feb. 25, 2005